

Association between somatosensory sensitivity and regional gray matter volume in healthy young volunteers: a voxel-based morphometry study

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Two-point discrimination (2PD) test reflects somatosensory spatial discrimination ability, but evidence on the relationship between 2PD and cortical gray matter (GM) volume is limited. This study aimed to analyze the relationship between cortical GM volume and 2PD threshold in young healthy individuals and to clarify the characteristics of brain structure reflecting the individual differences in somatosensory function. 2PD was measured in 42 healthy (20 females) volunteers aged 20–32 years using a custom-made test system that can be controlled by a personal computer. The 2PD of the right index finger measured with this device has been confirmed to show good reproducibility. T1-weighted images were acquired using a 3-T magnetic resonance imaging scanner for voxel-based morphometry analysis. The mean 2PD threshold was 2.58 ± 0.54 mm. Whole-brain multiple regression analysis of the relationship between 2PD and GM volume showed that a lower 2PD threshold (i.e. better somatosensory function) significantly correlated with decreased GM volume from the middle temporal gyrus to the inferior parietal lobule (IPL) in the contralateral hemisphere. In conclusion, a lower GM volume in the middle temporal gyrus and IPL correlates with better somatosensory function. Thus, cortical GM volume may be a biomarker of somatosensory function.

Key words: gray matter; inferior parietal lobe; middle temporal gyrus; 2-point discrimination; VBM.

Introduction

Somatosensory stimulation induces activity in various cortical areas, including the primary somatosensory cortex (S1), secondary somatosensory cortex (S2), posterior parietal cortex, and primary motor cortex (Inui et al. 2004). In addition to these areas, the premotor cortex, supplementary motor cortex, presupplementary motor cortex, dorsolateral prefrontal cortex (DLPFC), inferior frontal gyrus (IFG), insular cortex, inferior parietal lobule (IPL), supramarginal gyrus, angular gyrus, superior parietal lobule, interparietal sulcus (IPS), hMT/V5, temporoparietal junction (TPJ), and cerebellum are also activated during somatosensory discrimination tasks (Gao et al. 1996; Van Boven et al. 2005; Kitada et al. 2006; Pleger et al. 2006; Li Hegner et al. 2010; Wacker et al. 2011; van der Zwaag et al. 2013; van Kemenade et al. 2014; Li Hegner et al. 2015; Sarasso et al. 2018). The brain structure changes with training and with long-term experience. For example, the gray matter (GM) volume of the hMT/+V5 area, occipito-parietal areas, and

dorsal parietal cortex increases with juggling practice (Draganski et al. 2004; Boyke et al. 2008; Gerber et al. 2014; Sampaio-Baptista et al. 2014). Meanwhile, those of the lingual gyrus and IFG increase with a prolongation of flight time in pilots (Qiu et al. 2021). Furthermore, specific areas increase in musicians (Gaser and Schlaug 2003), typists (Cannonieri et al. 2007), and athletes (Bezzola et al. 2011; Schlaffke et al. 2014). Moreover, the GM volume of the posterior hippocampus is increased and that of the anterior hippocampus is decreased in taxi drivers (Maguire et al. 2000) and dancers (Hufner et al. 2011). Additionally, shadowing, reading, and cognitive training reduce GM volume in specific areas (Takeuchi et al. 2011a, 2011b; Maruyama et al. 2018; Takeuchi et al. 2021). Collectively, these findings indicate that it may be possible to predict somatosensory function from GM volume of cortical areas involved in somatosensory information processing; however, the relationship between somatosensory function and GM volume in untrained healthy individuals has not been clarified.

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Two-point discrimination (2PD) has been widely used to evaluate spatial acuity both clinically and in research on somatosensory perception. Several cortical areas, such as the IPS, IPL, supramarginal gyrus, anterior cingulate cortex, prefrontal gyrus, IFG and S1, anterior insula, and cerebellar vermis, are involved in 2PD (Akatsuka et al. 2008). Further, 2PD thresholds are declined (sensory function is improved) when transcranial alternation current stimulation is applied to the posterior parietal cortex (Yokota et al. 2021). Interestingly, Schmidt-Wilcke et al. 2018 reported that people with lower 2PD thresholds (better sensory function) have larger GM volumes in the thalamus and S1 and that repetitive electrical stimulation to the fingertip increases the volume of the parietal operculum and improves 2PD function. However, the relationship between 2PD and cortical GM volume has only been reported by Schmid-Wilcke et al., and thus, the reproducibility needs to be verified.

This study aimed to analyze the relationship between cortical GM volume and 2PD threshold in young healthy individuals and to clarify the brain structural characteristics reflecting the individual differences in somatosensory function.

Material and methods

Study design and participants

This voxel-based morphometry (VBM) study recruited 42 healthy volunteers (22 male and 20 female) aged 20–32 years (mean \pm standard deviation [SD]: 22.1 ± 2.2 years). None of the participants reported taking any drugs or medications which could affect central nervous system function. Handedness was assessed using the Edinburgh Handedness Inventory (39 right-handed, 3 left-handed, mean \pm SD: 73.2 ± 44.6) (Oldfield 1971). This study was approved by the Ethics Committee of Niigata University of Health and Welfare and was conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent before participation.

2PD measurement

The 2PD of the right index finger was measured with the participants seated in a resting position on a chair with a backrest. The right shoulder and elbow joints were placed in the slightly flexed position, whereas the forearm was positioned in a pronated position. The participants were instructed to relax and look at a fixed point approximately 1.5 m in their front. A custom-made 2-point tactile stimulator (Takei-kiki, Niigata, Japan), which allows detailed control of stimulation conditions (pin elevation speed, stimulation depth, and pin distance) by a personal computer, was used to measure 2PD threshold. The stimulus conditions were set at the following parameters based on the optimal measurement conditions of 2PD obtained in our previous study (Yokota et al. 2020): speed, 10.0 mm/s; penetration depth, 1.0 mm; and presentation time, 1.0 s. We have previously confirmed that the 2PD

measured using this device shows good reproducibility (Yokota et al. 2020). 2PD measurements consisted of 16 blocks, and a total of 10 types of stimuli to the right index finger pad, including 1 point (0 mm between stimulus pins) or 2 points (9 types of stimuli ranging from 1 to 5.0 mm at 0.5-mm interpin intervals), were presented randomly in each block. We explained that the 2 points should only be considered if they could be clearly identified as 2 points, whereas other vague stimuli and 1 point should be defined as 1 point. The participants were also instructed to respond by pushing the button held in their left hand when they recognized the stimulus. To analyze the data, the distance between the pins and the correct answer rate were plotted with a logistic regression line fitted using MATLAB (Matlab R2020a, MathWorks, Natick, MA). Thresholds at the correct rates of 50% as 2PD threshold were calculated based on the psychophysical curve using logistic regression analysis.

Magnetic resonance imaging data acquisition

Magnetic resonance data were acquired using a 3 T Vantage Galan magnetic resonance imaging (MRI) scanner (Canon Medical Systems, Tochigi, Japan) with a 32-channel head coil (QD coil, 32ch head SPEEDER, Atlas SPEEDER head/neck). The head was fixed using a head position pad to prevent motion artifacts. Moreover, headphones were used to reduce discomfort from loud noises. Anatomical images were acquired using a T1-weighted 3D magnetization-prepared rapid gradient echo sequence with the following parameters: inversion time = 900 ms, repetition time = 5.8 ms, echo time = 2.7 ms, flip angle = 9° , slice thickness = 1.2 mm, field of view = 23×23 cm², scan matrix = 256×256 , number of slices = 160, and slice gap = nongap.

Structural analysis

Image preprocessing and VBM were performed using SPM12 (Statistical Parametric Mapping, Wellcome Department of Imaging Neuroscience Group, London, United Kingdom; <http://www.fil.ion.ucl.ac.uk/spm>) implemented in Matlab R2020a (MathWorks). The T1-weighted images used for the analysis were visually checked for motion artifacts. The AC-PC line was corrected automatically using the Matlab script for automatic AC-PC setting (<http://www.nemotos.net/?p=17>). The T1-weighted images were segmented into GM, white matter, and cerebrospinal fluid after bias correction (bias regularization: light; bias full-width at half-maximum [FWHM] cut-off: 60 mm). The warping functions generated by the Diffeomorphic Anatomical Registration Through Exponentiated Lie Algebra (DARTEL) algorithm were used to spatially normalize to Montreal Neurological Institute space and modulate them using Jacobian determinants derived from spatial normalization (Ashburner 2007). The customized template image for DARTEL was created based on 42 participants. We applied 8-mm FWHM Gaussian kernel for spatial smoothing in the analysis. The sum of the

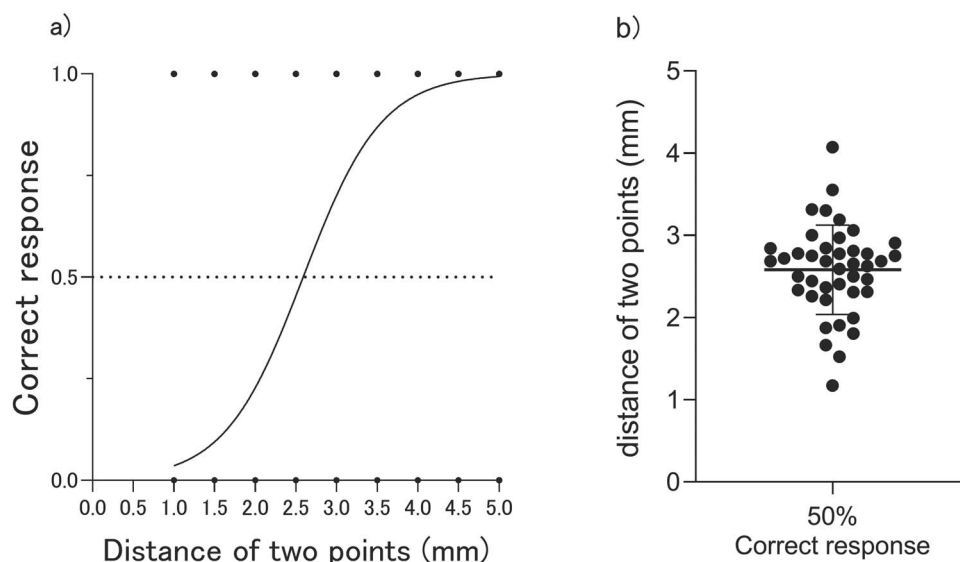


Fig. 1. Results of 2PD measurements. (a) Mean psychophysical curve in 2PD measurement for all participants. (b) Individual 2PD threshold for all participants.

total GM and white matter volumes was calculated as the total brain volume.

Statistical analysis

First, regression analysis was performed using the multiple regression model implemented in SPM12 to identify the brain regions associated with the independent variables (2PD). In the regression model, total brain volumes, age, and handedness were entered as covariates. The correction of the multiple comparison was carried out as follows: statistical parametric maps set thresholds at $P < 0.001$ (uncorrected voxel level). The whole-brain analysis was corrected for multiple comparisons ($P < 0.05$, correcting at cluster level, using family-wise error [FWE] correction). Voxel-by-voxel FWE corrections of statistical results are often too conservative for whole-brain analyses. Therefore, when no significant associations were found, $P < 0.001$ (uncorrected voxel level) and expected voxels per cluster (k) > 89 contiguous voxels were used to reduce the probability of a type II statistical error. MRICron software (www.people.cas.sc.edu/rorden/mricron) was used to illustrate VBM results.

Second, the regional GM volume of each brain region was calculated using the mask image created with the Automatic Anatomical Labeling (AAL) atlas (Tzourio-Mazoyer et al. 2002) included in the WFU_PickAtlas software version 3.0.5 (NeuroImaging Tools & Resources Collaboratory, https://www.nitrc.org/projects/wfu_pickatlas/). All 116 mask images (54 images in the right and left hemispheres and 8 images in the cerebellar vermis) were created, and GM volume in each region was normalized to each participant's total brain volume. The relationship between 2PD threshold and GM volume in each cortical region was analyzed with Pearson correlation analysis using IBM SPSS statistics version 24.0 (IBM, New York). Statistical significance was set at a P value of < 0.01 .

Results

The sigmoid curve of the 2PD test is shown in Fig. 1a. The 2PD threshold was 2.58 ± 0.54 mm (mean \pm SD, Fig. 1b). There were no sex differences in 2PD thresholds (male: 2.65 ± 0.58 mm; female: 2.50 ± 0.50 mm). The left middle temporal gyrus to the IPL was positively correlated with the 2PD threshold. The lower the GM volume in this area, the lower the 2PD threshold (better sensory function) ($P < 0.05$, correcting at cluster level, using FWE correction, Table 1 and Fig. 2). Meanwhile, a region in the left cerebellum was found to correlate negatively with the 2PD threshold, although it could not endure multiple corrections ($P = 1.51\text{E-}05$, uncorrected, Table 1 and Fig. 2).

Table 2 shows the results of correlation analysis between the 2PD threshold and GM volume in each regional area, which were calculated using the mask image created with the AAL atlas. Overall, 6 of the 116 regions showed a positive correlation with the 2PD threshold ($P < 0.01$); that is, the lower the 2PD threshold (better sensory function), the lower the GM volume. These 6 regions were the left middle temporal gyrus, left superior frontal gyrus (dorsolateral), left IPL, left primary motor cortex, right middle frontal gyrus, and right middle temporal gyrus (Table 2 and Fig. 3). Meanwhile, the left cerebellar lobule VIII, right cerebellar crus II, and right cerebellar lobule VII showed a negative correlation with the 2PD threshold ($P < 0.01$); that is, the lower the 2PD threshold (better sensory function), the higher the GM volume (Table 2 and Fig. 3).

Discussion

Evidence on the relationship between 2PD and cortical GM volume is limited. The results of whole-brain analysis in the current study showed that a low 2PD threshold

Table 1. Cortical regions correlated with the 2PD threshold.

		Cluster level			Peak level			MNI coordinates		
		<i>p</i>	<i>K_E</i>	<i>p</i>	<i>T</i>	<i>Z</i>	<i>p</i>	<i>x, y, z (mm)</i>		
Anatomical region		(FWE)	size	(unc)	value	score	(unc)	<i>x</i>	<i>y</i>	<i>z</i>
Positive ^a	Lt. middle temporal gyrus	0.00	1679.0	0.00	4.759	4.177	0.000	−56	−50	12
	Lt. IPS (hIP1)-IPL				4.702	4.136	0.000	−42	−53	38
	Lt. IPL				4.668	4.112	0.000	−56	−66	32
Negative ^b	Lt. cerebellum (crus I)	0.87	88.0	0.29	4.174	3.754	0.000	−53	−59	−30

Lt, left; unc, uncorrected; MNI, Montreal Neurological Institute. ^a $P < 0.05$, correcting at cluster level, using FWE correction. ^b $P < 0.001$ (uncorrected voxel level) and expected voxels per cluster (k) > 89 contiguous voxels.

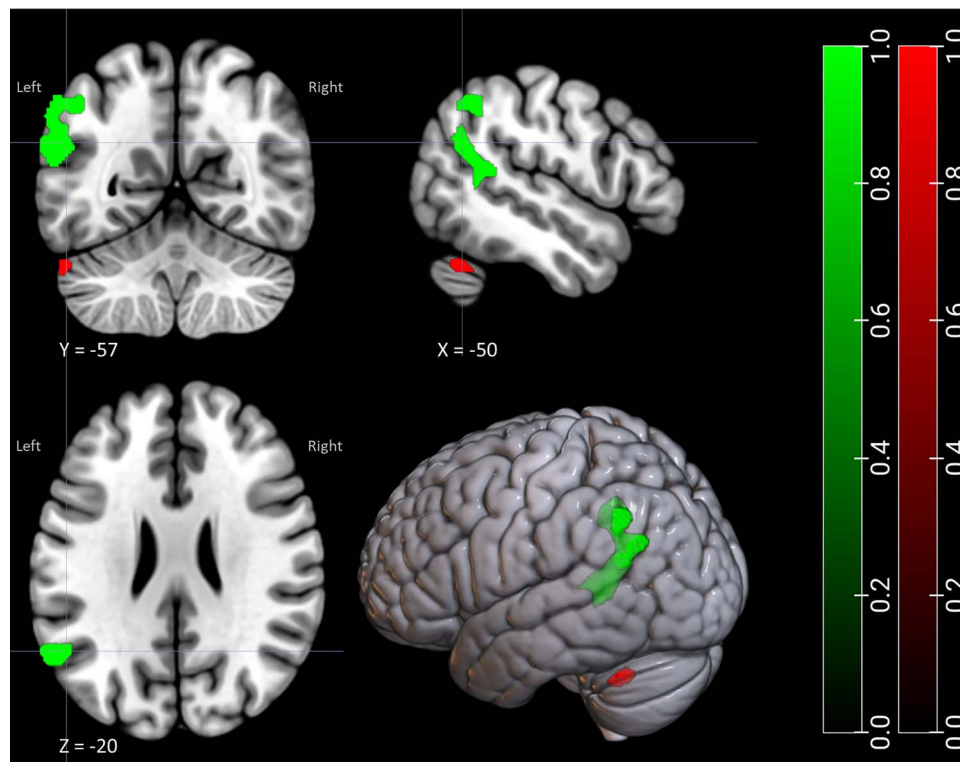


Fig. 2. Association between 2PD threshold and GM volume based on VBM analysis. Clusters in green indicate a significant positive association with 2PD threshold; that is, the lower the GM volume, the lower the 2PD threshold (higher somatosensory function). Clusters are focused in the left middle temporal gyrus and IPL ($P < 0.05$, correcting at cluster level using FWE correction). Clusters in red indicate a negative association; that is, the higher the GM volume, the lower the 2PD threshold (higher somatosensory function). Clusters are focused in the left cerebellum crus I ($P < 0.001$, uncorrected voxel level, with expected voxels per cluster, k , > 89 contiguous voxels).

(i.e. better sensory function) was associated with lower GM volume from the middle temporal gyrus to the IPL in the contralateral hemisphere. Furthermore, analysis of ALL labels revealed that GM volumes in the contralateral middle temporal gyrus, IPL, superior frontal gyrus (dorsolateral), primary motor cortex, ipsilateral middle temporal gyrus, and middle prefrontal cortex were significantly correlated with the 2PD threshold, indicating that the better the sensory function, the lower the GM volume. The current study findings are useful to further elucidate the relationship between individual differences in somatosensory function and brain structure and may contribute to understanding the characteristics of individuals with sharp somatosensory functions.

The middle temporal gyrus and IPL showed the strongest positive correlation with the 2PD threshold;

that is, the better the performance, the smaller the GM volume in these regions. This may be due to the presence of the hMT+/V5 area and the TPJ in the posterior superior portion of the middle temporal gyrus. The hMT+/V5 area, which has been reported to be active during dynamic tactile stimulation, contributes to the performance of somatosensory function (Summers et al. 2009; Wacker et al. 2011; van Kemenade et al. 2014). In addition, the TPJ is not only activated during somatosensory discrimination tasks (Van Boven et al. 2005) but has also been reported to be associated with attentional function (Geng and Vossel 2013; Dugue et al. 2018). Given that attention alters the activity in the S2 cortex, which is involved in somatosensory information processing (Hsiao et al. 2002), it is possible that the participants with good somatosensory performance also had better

Table 2. Brain regions with significant correlation between GM volume and 2PD threshold ($n = 116$ brain regions).

Anatomical region ^b	Left hemisphere		Right hemisphere	
	<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Central region				
Precentral gyrus	0.394	a	0.0099	0.080
Postcentral gyrus	0.117		0.4600	0.305
Rolandic operculum	0.206		0.1905	0.219
Frontal lobe				
Lateral surface				
Superior frontal gyrus, dorsolateral	0.415	a	0.0063	0.377
Middle frontal gyrus	0.292		0.0604	a
IFG, opercular part	0.103		0.5179	0.076
IFG, triangular part	−0.010		0.9513	0.083
Medial surface				
Superior frontal gyrus, medial	0.255		0.1032	0.115
Supplementary motor area	0.127		0.4225	0.199
Paracentral lobule	0.278		0.0745	0.185
Orbital surface				
Superior frontal gyrus, orbital part	0.069		0.6644	−0.059
Superior frontal gyrus, medial orbital	0.001		0.9974	−0.026
Middle frontal gyrus, orbital part	−0.047		0.7694	−0.089
IFG, orbital	0.073		0.6438	0.249
Gyrus rectus	0.192		0.2238	0.038
Olfactory cortex	0.189		0.2303	0.161
Temporal lobe				
Lateral surface				
Superior temporal gyrus	0.274		0.0787	0.372
Middle temporal gyrus	0.545	a	0.0002	a
Inferior temporal gyrus	0.329		0.0334	0.349
Heschl gyrus	0.120		0.4476	0.190
Parietal lobe				
Lateral surface				
Superior parietal gyrus	0.331		0.0325	0.326
Inferior parietal gyrus	0.407	a	0.0074	−0.115
Angular gyrus	0.378		0.0137	−0.040
Supramarginal gyrus	0.044		0.7844	0.269
Medial surface				
Precuneus	0.115		0.4689	0.022
Occipital lobe				
Lateral surface				
Superior occipital gyrus	0.131		0.4087	−0.070
Middle occipital gyrus	0.105		0.5083	−0.045
Inferior occipital gyrus	0.168		0.2887	0.044
Medial and inferior surface				
Cuneus	−0.095		0.5506	−0.137
Calcarine fissure and surrounding cortex	−0.290		0.0626	−0.225
Lingual gyrus	0.106		0.5055	−0.015
Fusiform gyrus	0.101		0.5236	0.104
Limbic lobe				
Temporal pole: superior temporal gyrus	0.139		0.3784	0.129
Temporal pole: middle temporal gyrus	0.073		0.6473	0.291
Anterior cingulate and paracingulate gyri	0.276		0.0768	0.349
Median cingulate and paracingulate gyri	0.184		0.2439	0.253
Posterior cingulate gyrus	0.278		0.0743	0.059
Hippocampus	0.008		0.9614	0.102
Para hippocampus gyrus	−0.029		0.8532	0.154
Insula				
Insula	−0.027		0.8647	0.129
Subcortical gray nuclei				
Amygdala	−0.019		0.9073	0.073
Caudate nucleus	0.002		0.9902	−0.004

(Continued)

Table 2. Continued.

Anatomical region ^b		Left hemisphere		Right hemisphere	
		<i>r</i>	<i>P</i>	<i>r</i>	<i>P</i>
Cerebellum	Putamen	−0.013	0.9342	−0.024	0.8793
	Pallidum	−0.029	0.8559	−0.107	0.4995
	Thalamus	0.016	0.9191	−0.066	0.6790
	Hemisphere				
	Cerebellum crus I	−0.369	0.0161	−0.243	0.1205
	Cerebellum crus II	−0.275	0.0774	−0.408	a 0.0074
	Cerebellum III	−0.050	0.7553	−0.182	0.2490
	Cerebellum IV–V	−0.109	0.4917	−0.204	0.1939
	Cerebellum VI	−0.146	0.3565	−0.187	0.2347
	Cerebellum VII	−0.377	0.0138	−0.394	a 0.0097
	Cerebellum VIII	−0.492	a 0.0009	−0.36	0.0194
	Cerebellum IX	−0.303	0.0514	−0.216	0.1704
	Cerebellum X	−0.187	0.2345	0.006	0.9683
	Vermis				
	Vermis I–II	0.079	0.6177		
	Vermis III	−0.190	0.2273		
	Vermis IV–V	−0.234	0.1360		
	Vermis VI	−0.171	0.2802		
	Vermis VII	−0.141	0.3726		
	Vermis VIII	−0.325	0.0358		
	Vermis IX	−0.328	0.0342		
	Vermis X	−0.163	0.3014		

^a*P* < 0.01. ^bEach brain region is calculated using the mask image created with the AAL atlas (Tzourio-Mazoyer et al. 2002).

attentiveness to stimulation. The IPS and angular gyrus, located postero-inferiorly to the IPL, also play important roles in attentional function (Rushworth and Taylor 2006; Chechlacz et al. 2012) and perceptual decision-making (Ploran et al. 2007; Tosoni et al. 2008; Ho et al. 2009; Studer et al. 2014; Wu et al. 2021). The 2PD test requires the test administrator's judgment regarding to whether a given stimulus should be allotted 1 or 2 points. Therefore, the neural basis of perceptual decision-making may be involved in the 2PD threshold. Moreover, the IPL, superior frontal gyrus (dorsolateral), and primary motor cortex are also activated during somatosensory stimulation or somatosensory discrimination tasks (Inui et al. 2004; Van Boven et al. 2005; Kitada et al. 2006; Pleger et al. 2006; Terumitsu et al. 2009; van Kemenade et al. 2014; Gomez et al. 2021; Jung et al. 2021).

Regarding the relationship between GM volume and performance, some reports indicate that training and specific experiences increase GM volume in certain regions, while others cause a decrease. For example, mental arithmetic training decreases the GM volume in the superior temporal gyrus and DLPFC (Takeuchi et al. 2011b), while oral reading training decreases the GM volume in the superior temporal gyrus (Takeuchi et al. 2011a; Maruyama et al. 2018). Moreover, lower GM volumes in specific areas are reportedly associated with better music perception (Hyde et al. 2007; Bermudez et al. 2009) and higher concentration (Kanai et al. 2011). Furthermore, the GM volume in the inferior temporal gyrus, middle temporal gyrus, and IPL has recently been identified as being increased in autism

spectrum disorder with impaired attention (Cai et al. 2018; Kobayashi et al. 2020; Lukito et al. 2020; Yaxu et al. 2020), and this has been attributed to brain overgrowth (Kobayashi et al. 2020). Thus, lower GM volume is reportedly associated with better performance. Furthermore, healthy individuals with higher rectal sensitivity (lower threshold) to visceral pain reportedly have lower GM volumes in the thalamus, insula, amygdala, and cingulate gyrus (Elsenbruch et al. 2014). Moreover, a lower threshold to thermal stimuli (more sensitive) denotes a lower GM volume in the IPL, IPS, posterior cingulate gyrus, and S1 (Erpelding et al. 2012). Consistent with these reports, the current study found that the GM volume of the cerebral cortex involved in somatosensory information processing was smaller in individuals with more sharp somatosensory functions.

Although it is difficult to interpret the cellular and molecular events behind the GM volume calculated from human MR images, cell density, cell size, synaptic density, myelin sheath, glial cell size and number, capillaries, water content, and GABA_A receptor are thought to influence GM volume (Morrison and Hof 1997; Draganski et al. 2004; Zatorre et al. 2012; Pomares et al. 2017). However, it is unclear which of these factors affect the results of the current study, and thus, the reason for the negative correlation between sensory performance and GM volume is unclear. It is possible that the GM volume declines with growth (Sowell et al. 2003; Gogtay et al. 2004), that synaptic pruning in the cerebral cortex occurs during adolescence (Huttenlocher and Dabholkar 1997; Petanjek et al.

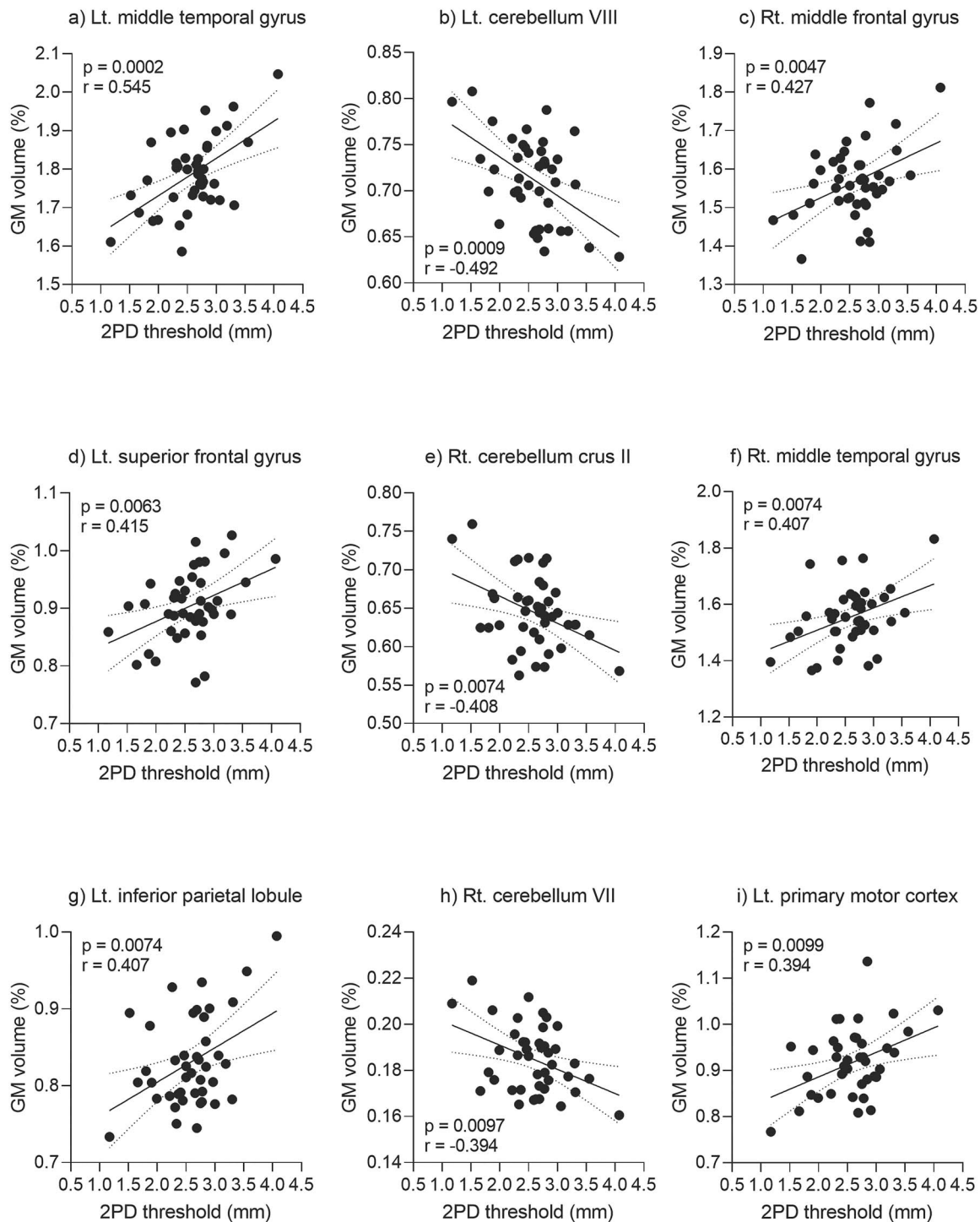


Fig. 3. Relationship between 2PD threshold and GM volume at each brain region that showed significant correlations with the 2PD threshold. Each region is calculated using the mask image created with the AAL atlas. A total of 6 regions positively correlate with the 2PD threshold ($P < 0.01$); that is, the lower the 2PD threshold (better sensory function), the lower the GM volume. Meanwhile, 3 regions negatively correlate with the 2PD threshold ($P < 0.01$); that is, the lower the 2PD threshold, the higher the GM volume. All these regions are found in the cerebellum. (a) Lt. middle temporal gyrus, (b) Lt. cerebellum VIII, (c) Rt. middle frontal gyrus, (d) Lt. superior frontal gyrus (dorsolateral), (e) Rt. cerebellum crus II, (f) Rt. middle temporal gyrus, (g) Lt. IPL, (h) Rt. cerebellum VII, and (i) Lt. primary motor cortex.

2011), and that removing weak synapses improves the computational performance in cortical regions (Chechik et al. 1999). Furthermore, the balloon model indicates that the stretching of the GM with myelin growth and GM thinning improves the ability to distinguish signals (Harasty et al. 2003; Seldon 2005, 2007).

Kanai et al. (2011) highlighted that a smaller volume as a result of pruning to remove inefficient synapses and neurons enables more efficient processing (Kanai and Rees 2011).

We agree with these ideas. However, many studies have reported increases in GM volume due to specific

experiences and training, such as in taxi drivers (Maguire et al. 2000), pilots (Qiu et al. 2021), dancers (Hufner et al. 2011), and jugglers (Draganski et al. 2004). Moreover, although the cause for this difference is unclear, it may be due to nonlinear changes in the GM volume which are influenced by the length and intensity of training, which decrease following an initial increase, as advocated by Takeuchi and colleagues (Takeuchi et al. 2011b). The present study assessed healthy young adults with no special training; thus, the changes were not an effect of short-term training. Specifically, the somatosensory function in this study might have been due to growth-related loss of synapses or decrease in GM volume from myelin growth rather than a temporary change in the GM volume due to a short training period. However, these are only speculations, and they need to be verified in future animal experiments.

The present study found a negative correlation between 2PD threshold and cerebellar GM volume, indicating that the better the sensory function, the larger the cerebellar GM volume. However, the whole-brain analysis could not withstand multiple comparison correction, and thus, the results should be interpreted with caution. The cerebellum is not only important for movement and speech, but it is also activated in somatosensory stimulation or somatosensory discrimination tasks (Gao et al. 1996; Pastor et al. 2004; Kitada et al. 2006; van der Zwaag et al. 2013; van Kemenade et al. 2014). Furthermore, it is active during cognitive tasks (Stoodley and Schmahmann 2010, 2018; Stoodley et al. 2012; Guell et al. 2018). These findings indicate that the relationship between 2PD threshold and the cerebellar GM volume is reasonable. However, in contrast to the results for the cerebral cortex, there was a positive correlation between performance and GM volume in the cerebellum. The developmental process of the cerebellum differs from that of the cerebral cortex (Stoessel and Majewska 2021), which may account for this difference in 2PD threshold and GM volume relationship. However, the reason for this is unclear and requires further investigation.

Schmidt-Wilcke and others have reported that a lower 2PD threshold (better sensory function) indicates a larger thalamus and S1 volume (Schmidt-Wilcke et al. 2018); however, this was not observed in the present study. The thalamus volume calculated by VBM is somewhat less reproducible (Watanabe et al. 2021). This may explain why the results of the relationship between GM volume of the thalamus and 2PD reported by Schmidt-Wilcke et al. could not be reproduced. However, the reason for the lack of a significant correlation between S1 volume and the 2PD threshold in the current study is unclear, although this might have been due to the difference in the testing method for 2PD. Although we similarly measured 2PD with precision instruments and defined the 2PD threshold at 50%, the mean 2PD threshold was 2.58 mm in our study, whereas it was 1.59 mm in the study by Schmidt-Wilcke et al. This might

have influenced the results, but the specific cause is unknown.

A limitation of this study is that although VBM is an excellent tool for analyzing minute morphological changes in the human brain, the type of morphological change induced is unclear. Moreover, the correlation analysis of ALL labels was not corrected for multiple comparisons to reduce the probability of type II statistical errors. However, all regions that correlated with the 2PD threshold ($P < 0.01$) are involved in somatosensory information processing, and the results are reasonable and complementary to the results of the whole-brain analysis. Furthermore, because we only included young healthy individuals, it is unclear whether similar trends exist in other age groups or in patients with neurological disorders. Further research is needed in these populations.

In conclusion, whole-brain analysis indicates that a lower GM volume in the middle temporal gyrus and IPL leads to a better somatosensory function. Thus, cortical GM volume may be a biomarker for somatosensory function. The results of this study can contribute to the understanding of individual differences in somatosensory function in young healthy subjects.

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Data and code availability statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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